

**REMARKS**

Claims 1-4, 7, 8, 11-20, 52, 53 and 56 are currently pending in this application. Applicants respectfully request reconsideration of pending claims 1-4, 7, 8, 11-20, 52, 53 and 56

**I. Rejection of Claims Under 35 U.S.C. § 103(a)**

**A. Rejection of Claims 1-4, 7, 8, 11-20, and 52 Over Boschetti**

Claims 1-4, 7, 8, 11-20, and 52 remain rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Boschetti (U.S. Patent No. 5,635,215).

Applicants respectfully traverse this ground of rejection for essentially the reasons of record.

The U.S. Supreme Court has recently addressed the test for obviousness under 35 U.S.C. § 103. *KSR International Co. v. Teleflex Inc.*, No. 04-1350, 550 U.S. \_\_\_ (2007). In *KSR*, the Supreme Court rejected the Federal Circuit's *rigid application* of the ‘teaching, suggestion, motivation’ test (“the TSM test”) in determining obviousness in the particular case in question. *Id.*, *slip op.* p. 11. According to the Supreme Court, the correct standard to apply is set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966). *Id.*, *slip op.* p. 2. However, the *KSR* decision indicated that while the TSM test is not the sole method for determining obviousness, it may still be a factor. *Id.* *slip op.* p. 14 (“When it first established [the TSM test], the Court...captured a helpful insight.”). Indeed, on May 3, 2007, the Deputy Commissioner of Patents circulated a memorandum to the Technology Center Directors (“USPTO Memorandum”) pointing out that the TSM test was not completely abolished in *KSR*.

The *Graham* factual inquiries, which establish a guide for determining obviousness, are: (1) determine the scope and contents of the prior art; (2) ascertain the differences between the prior art and the claims at issue; (3) resolve the level of ordinary skill in the pertinent art; and (4) evaluate any evidence of secondary considerations. *KSR*, *slip op.* p. 2 (*citing Graham*, 383 U.S. at 15-17).

The instant claims are not obvious because the microspheres disclosed in Boschetti differ from microspheres recited in the instant claims. Furthermore, the scope and content of Boschetti does not provide a reason that would have prompted one of ordinary skill in the art to modify the teachings of Boschetti to arrive at the methods of the instant claims.

The Examiner correctly acknowledges that Boschetti does not expressly disclose any of the following features recited by the claims (Office Action, page 2):

- (1) that the polymer is an anionic polymer;
- (2) that the compositions would be injectable through needles of about 18-26 gauge;
- (3) the particular amount to the particles in the composition; and/or
- (4) the particular agents in the composition.

Nonetheless, the Examiner opines that it would have been *prima facie* obvious to a person of ordinary skill in the art to use an anionic polymer as the hydrophilic polymer and to adjust the particle size within the disclosed range so that the composition would be suitable for injection with any needle required in the method (office Action, page 3).

While it is true that Boschetti *generally* teaches microspheres comprising a hydrophilic acrylic copolymer for vascular embolization, the reference does not teach or make obvious the claimed swellable microspheres for tissue bulking comprising (1) an anionic polymer that is (2) crosslinked in an amount of from about 0.5% to about 20% and can (3) increase its weight by at least about 20 times its original dry weight upon contacting water. See, e.g., *Ex parte Obukowicz*, 27 USPQ2d 1063, 1065 (Bd. Pat. App. & Int’f 1992) (prior art which provides only general guidance and is not specific as to the particular form of the claimed invention and how to achieve it does not render the invention unpatentably obvious).

Regarding the term “swellable,” as those skilled in the polymer art would appreciate, not all hydrophilic acrylic polymers are swellable, as recited in claim 1 of the instant

invention. Additionally, not all hydrophilic acrylic polymers can increase in weight by at least about 20 times the original dry weight upon contacting water (*i.e.*, high water absorbing polymers) as recited in instant claim 1. Further, because Boschetti teaches that one problem to avoid is that some types agents cause “sticking of catheters” (col. 1, lines 31-34) or “blocking of the systems necessary for injection” (col. 6, lines 49-52), one of skill in the art, upon reading Boschetti, may consider avoiding the use of certain swellable compositions, especially those that swell by at least about 20 times the original dry weight upon contacting water, in order to avoid potential problems such as needle clogging or sticking. Thus, the Applicants maintain that Boschetti actually teaches away from the instant invention.

In addition, the Boschetti reference extensively discloses the benefits of cationic microspheres-- rather than anionic microspheres of the instant invention--as well as microspheres mixed or coated with cell adhesion promoters in order to engender cell adhesion properties to the injected material. Not only is the term “anionic” (or even the term “negative charge”) entirely absent, instead Boschetti discloses at length the numerous advantages of the cationic microspheres.

The Examiner acknowledges that Boschetti “prefer[s] natural or cationic polymers, but cites claim 1 of Boschetti as encompassing all hydrophilic acrylic polymers, regardless of charge. However, when read in context, claim 1 of Boschetti recites hydrophilic, acrylic copolymer microspheres that are coated with a cell adhesion promoter (Office Action, page 5). Indeed, the use of hydrophilic microspheres that are cationic in charge is taught throughout Boschetti:

- Col. 2, lines 17-19: “The presence of a cationic charge on the surface of the microsphere makes it possible to initiate and improve cell adhesion.”
- Col. 1, lines 46-48: “One object of the invention resides more specifically in the use of microspheres comprising an hydrophilic acrylic copolymer coated with a cell adhesion promoter.”
- Col. 4, lines 56-60 (discussion of the qualities of the prepared microspheres of Example 1): “Those microspheres,...possess the characteristics desired for

embolization, including a marked cationic charge and an effective adhesion agent (gelatin or denatured collagen).”

Taken individually or together, one skilled in the art would understand from the disclosure of Boschetti that, without the cationic charge, there will be poor cell adhesion. Along the same line, Boschetti mentions that one problem with polystyrene spheres (used as a comparative control) is that they do not stick well to the surrounding cells: “on the 8th day, the thickness of the cell reaction covering the spheres of the invention is almost three times greater than that covering the polystyrene spheres (Col. 6, lines 23-26), and that the “vascular injection with the polystyrene spheres is difficult and clusters are formed....” Boschetti concludes the comparative experiment by noting that: “the microspheres of the invention are more manageable and more effective as adhesive agent” (Col. 6, lines 31-32).

Further the Boschetti compositions are generally intended for injection into veins for vascular embolization. The microspheres are packed into a walled structure (the vein), and are thus not as likely to be dispersed into the surrounding tissues. However, one of skill in the art interested in tissue bulking, rather than a walled structure such as a vein, would be even more interested in ensuring that the microspheres do not move about. Thus, one of skill in the art, would not be likely to choose anionic microspheres as recited in the instant invention, because Boschetti teaches that cationic microspheres, or microspheres with cell adhesion promoters, have better cell adhesion properties in order to keep the microspheres in the injected location. Accordingly, it would not be obvious to one of skill in the art, upon reading Boschetti, to consider that the claimed invention would be effective for tissue bulking.

Furthermore, in *KSR*, the references cited by the Examiner provided the patentee with all the elements of the claimed invention—the claimed invention was obtained merely by combining the references “like pieces of a puzzle.” *KSR, slip op.*, pp. 16-17. However, the instant case is distinguishable because Boschetti does not provide each element of the instant claims, namely, a swellable microsphere comprising (1) an anionic polymer that is (2) crosslinked in an amount of from about 0.5% to about 20% and can (3) increase its weight by at least about 20 times its original dry weight upon contacting water, as recited in the claims. Indeed, as mentioned above, Boschetti discloses that cationic microspheres are preferred due

to the ability to improve cell adhesion (see, *e.g.*, Col. 2, lines 11-37; Col. 3, lines 3-10; Col. 4, lines 57-60).

Therefore, because Boschetti does not disclose the injectable compositions of the instant claims, and because substantial differences exist between the instant claims and the scope and content of Boschetti, the instant claims are not obvious over this reference.

Further, the teachings of Boschetti would not prompt a person of ordinary skill to combine the elements to arrive at the instant claims.

In *KSR*, the Supreme Court emphasized that the “combination of familiar elements according to known methods is likely to be obvious when it yields no more than predictable results.” *KSR*, *slip op.* p. 12. However, the Court cautioned that “[f]ollowing these principles may be more difficult in other cases...because the claimed subject matter may involve more than the simple substitution of one known element for another...” *Id.*, *slip op.* p. 14. Further, “it can be important to *identify a reason* that would have prompted a person of ordinary skill...to combine the elements in the way the claimed new invention does.” *Id.*, *slip op.* p. 15 (emphasis added); *see also* USPTO Memorandum (“it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.”).

As established above, the instant case involves more than the “simple substitution” of known elements in the prior art. Therefore, the Examiner must provide a reason why one of ordinary skill in the art would use the teachings of Boschetti and somehow arrive at the microspheres of the instant claims. The Examiner merely relies on the alleged overlap of certain elements of the microspheres of Boschetti with those of the instant claims. (Office Action, pages 2-5). However, the Examiner has provided no basis for the allegation that the instant claims are obvious over Boschetti, and the Examiner’s burden to support a rejection on the grounds of obviousness with explicit, articulate reasoning remains. *KSR*, *slip op.* p. 14 (*citing In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006); *see also* USPTO Memorandum).

Further, because the cationic microspheres disclosed in Examples of Boschetti were *effective for vascular embolization*, one skilled in the art would have had no motivation whatsoever to use the claimed microspheres comprising *any anionic* polymer, *much less* an

anionic polymer that is crosslinked in an amount of from about 0.5% to about 20% and can increase its weight by at least about 20 times its original dry weight upon contacting water for vascular embolization much less for tissue bulking, which is a completely unrelated field.

For at least these reasons, Applicants submit that claims 1-4, 7, 8, 11-20 and 52 are non-obvious over Boschetti. Accordingly, reconsideration and withdrawal of this ground of rejection is respectfully requested.

**B. Rejection of Claims 53 and 56 Over Boschetti and Tahara**

Claims 53 and 56 remain rejected as allegedly being unpatentable over Boschetti in view of Tahara (U.S. Patent No. 5,298,570) ("Tahara").

Applicants respectfully traverse this ground of rejection for essentially the reasons of record.

As discussed above, in *KSR*, the Supreme Court cautioned that "the claimed subject matter may involve more than the simple substitution of one known element for another..." *Id.*, *slip op.* p. 14. Further, "it can be important to *identify a reason* that would have prompted a person of ordinary skill...to combine the elements in the way the claimed new invention does." *Id.*, *slip op.* p. 15 (emphasis added); *see also* USPTO Memorandum ("it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.").

The instant case involves more than the "simple substitution" of known elements in the prior art. Therefore, the Examiner must provide a reason why one of ordinary skill in the art would combine the teachings of Boschetti and Tahara and somehow arrive at the microspheres of the instant claims. Instead, the Examiner merely states that the substitution of a sodium acrylate / vinyl alcohol copolymer would be *prima facie* obvious because sodium acrylate / vinyl alcohol copolymers "were known" (Office Action, page 4). Accordingly, the Examiner has provided no basis for the allegation that the instant claims are obvious over Boschetti in view of Tahara, and the Examiner's burden to support a rejection on the grounds of obviousness with explicit, articulate reasoning remains. *KSR*, *slip op.* p. 14 (*citing In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006); *see also* USPTO Memorandum.

At the outset, Applicants submit that Tahara is in a non-analogous field. “[I]n order to rely on a reference as a basis for rejection of an applicant’s invention, the reference must either be in the field of applicant’s endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned.” *In re Oetiker*, 977 F.2d 1443, 1446 (Fed. Cir. 1992). *See also In re Clay*, 966 F.2d 656, 659 (Fed. Cir. 1992) (“A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor’s endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to an inventor’s attention in considering his problem.”). The present claims are related to injectable compositions suitable for tissue bulking. In stark contrast, Tahara is related to a biodegradable crosslinked polymer having a chelating effect and a function to disperse an oily substance and an inorganic substance hardly soluble in water, as well as a biodegradable medicine, which may be used involving discharge into environment at a final stage, such as a fiber-treating agent, an inorganic pigment dispersant and a water treatment agent. As such, Applicants submit that there would be no motivation for the ordinary skilled artisan to look to Tahara with respect to the art of tissue bulking.

Second, even assuming *arguendo*, that one of skill in the art would somehow review Tahara (Applicants maintain they would not), sodium acrylate/vinyl alcohol co-polymers would not be found suitable for tissue bulking because the Tahara compositions are taught to be both biodegradable and dispersible. These two qualities would not be pursued by one of skill in the art searching for a microsphere for tissue bulking, because 1) it would not be desirable to choose a composition that is taught to disperse readily, thus potentially moving far from the injection site and even potentially disfiguring the subject, and 2) it would not be desirable to choose a composition that is taught to be readily biodegradable, as the tissue bulking effect would quickly dissipate in the subject.

Thus, for at least these reasons, Applicants submit that claims 53 and 56 are non-obvious over Boschetti in view of Tahara. As such, Applicants respectfully request that this rejection be reconsidered and withdrawn.

## **II. Conclusion**

In view of the foregoing amendments and remarks, Applicants respectfully submit that this application is now in condition for immediate allowance. *If the Examiner disagrees,*

*Applicants respectfully request that the Examiner call the undersigned at the number listed below.*

A request for Continued Examination (RCE) Transmittal is also submitted herewith, which authorizes the PTO to deduct the estimated RCE fee of \$405.00 to Jones Day Deposit Account No. 50-3013, which reflects the Applicant's small entity status. Applicants believe no other fees are due in connection with this Amendment. However, if there are any fees due, please charge them to Deposit Account 50-3013. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should be charged to our Deposit Account. Also, please charge any fees underpaid or credit any fees overpaid to the same Deposit Account.

Respectfully submitted,

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